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FACILITY

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Abstract

The International Space Station (ISS) will support several facilities dedicated to scientific research. One such facility, the Biotechnology Facility (BTF), is sponsored by the Microgravity Sciences and Applications Division (MSAD) and developed at NASA's Johnson Space Center. The BTF is scheduled for delivery to the ISS via Space Shuttle in April 2005.

The purpose of the BTF is to provide (i) the support structure and integration capabilities for the individual modules in which biotechnology experiments will be performed, (ii) the capability for human-tended, repetitive, long-duration biotechnology experiments, and (iii) opportunities to perform repetitive experiments in a short period by allowing continuous access to microgravity.

The MSAD has identified cell culture and tissue engineering, protein crystal growth, and fundamentals of biotechnology as areas that contain promising opportunities for significant advancements through low-gravity experiments. The focus of this coordinated ground- and space-based research program is the use of the low-gravity environment of space to conduct fundamental investigations leading to major advances in the understanding of basic and applied biotechnology. Results from planned investigations can be used in applications ranging from rational drug design and testing, cancer diagnosis and treatment, and tissue engineering leading to replacement tissues.

Biotechnology Facility

The BTF is a single rack facility designed to meet those needs and requirements that are identified by the science community. It is envisioned as a continuously operating facility on ISS that accommodates investigations in cell science and tissue engineering, protein crystal growth, and bioseparations. The BTF

offers (i) long-duration microgravity conditions favorable for slow-growing protein crystals and tissue engineering; (ii) the opportunity to conduct multiple experiments with relatively short intervals between experiments; and (iii) a constant source of research materials such as protein crystals, microencapsulated drugs, and engineered tissues.

The BTF is modular in design, providing the flexibility to accommodate a wide range of biotechnology experiments. This design accommodates changes in experiment modules and analytical equipment in response to changes in either science priorities or technical advances. The facility will augment the Space Station laboratory resources by providing experiment control computers, heat elimination, and four types of research-grade gas (oxygen, carbon dioxide, nitrogen and argon).

The BTF has seven locations dedicated to experiment payloads (Figure 1). Each payload location is the size of one Space Shuttle middeck locker. Payloads can be designed to fit into standard single, double or quadruple lockers, and will be delivered to and from the ISS via Space Shuttle. The BTF can supply power to the payloads at either 28 V dc or 120 V ac. Two experiment modules can draw up to a maximum of 400 watts at any given time, with the remainder of locations being able to draw up to 170 watts.

The Johnson Space Center's Biotechnology Program has developed a ground-based emulation of the BTF, called the Mini-Payload Integration Center (Mini-PIC) (Figure 2). This system provides flight-approved scientists with a duplicate of the BTF's interfaces early in their experiment development process. Each Mini-PIC can accommodate two middeck-sized payloads and provides the same data acquisition & control system, power and data connections, as well as gas, water, and vacuum resources used in the BTF. The Mini-PIC is a working model with which researchers can build,

conduct, and evaluate their experiments in their own laboratories at their home institutions. The ability to integrate and test experiments on the ground in the same facilities they will use in flight both reduces risks and increases greater scientific returns from ISS.

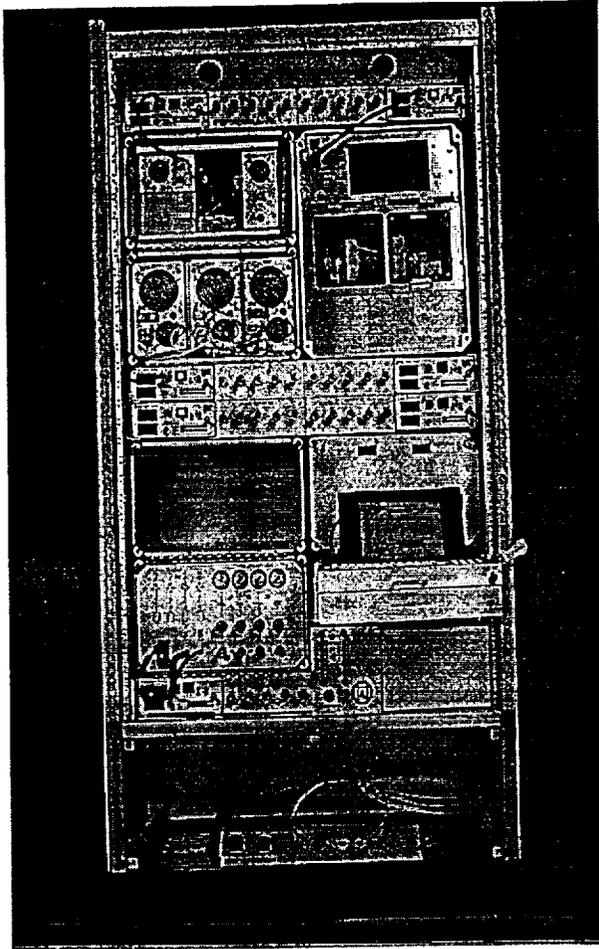


Figure 1. ISS Biotechnology Facility (BTF). The Cellular Biotechnology Program will provide a rack-level facility to the ISS to support experiments in cell science, protein crystallization, and separation science. This Biotechnology Facility (BTF) is currently planned to hold up to 7 biotechnology MLE payloads aboard ISS, and to provide power, gases, cooling, computers for payload operation and data archiving, video capture, and air and water purification. The BTF will include a Facility Control System (FCS) to operate the BTF and interface with each of the individual experiment modules. A truncated, risk-mitigation version of the BTF has operated onboard Mir.

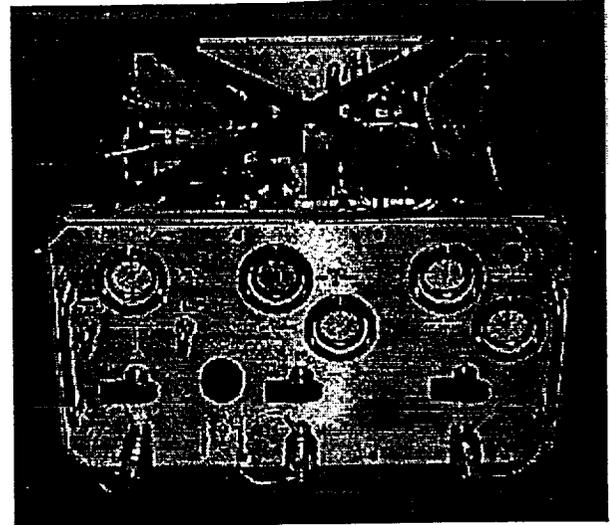
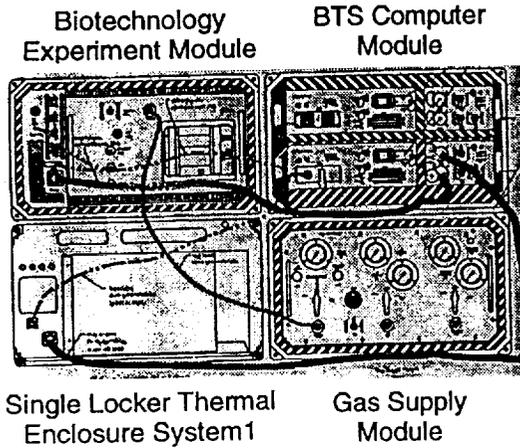


Figure 2. Mini-Payload Integration Center (Mini-PIC). The Mini-PIC is a small-scale 2 MLE emulation of the BTF for use by Principal Investigator's (PIs) in preparation for experiments on ISS. Experiment-specific hardware will be integrated into the Mini-PICs to emulate the experiment-to-BTF interfaces. This Mini-PICs will not only permit PIs to prepare and optimize their experiments for space flight, but will also be used to derive BTF requirements.

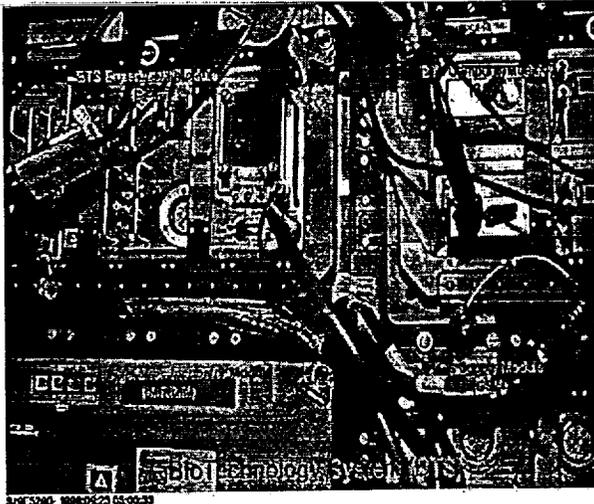
As further risk mitigation, we have successfully designed and operated a forerunner of the BTF on the Russian space station Mir. The BioTechnology System (BTS) was launched on *Priroda* in April 1996; the BTS contained the hardware and laboratory resources required supporting many long-duration science investigations planned for its 2-year operation aboard Mir (Figure 3). The long duration operation of the BTS Facility has enabled us to validate BTF concepts and systems, and to mitigate risk through on-orbit use of BTF components and verification of BTF procedures. In addition, the experience and results obtained from conducting fundamental science investigations in the BTS have been used to clarify the science requirements for the BTF on ISS and to optimize the BTF design.

BTS Facility Schematic

Biotechnology System Priroda Operational Configuration



Gas Supply Module for ISS



BTS (Facility on Mir)

Figure 3. Biotechnology System (BTS) Facility on Mir. BioTechnology System (BTS) used aboard MIR contained the hardware and laboratory resources required supporting long-duration science investigations. The experience and results obtained from conducting fundamental science investigations in the BTS are being used to clarify the science requirements for the BTF on ISS and to optimize BTF design.

Facility Hardware

Gas Supply Module Mir

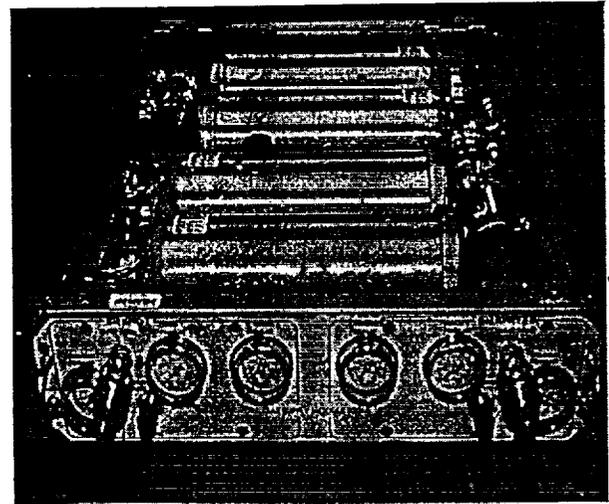


Figure 4. Gas Supply Modules (GSM)

Science Objective:

This hardware houses and provides N_2 , CO_2 and other gases at required concentrations and pressures for principal investigators to conduct cell science investigations in microgravity with the space bioreactors, EDU, HFB, and BSTC.

Operational Description:

The Gas Supply Module used on Mir was a full middeck locker while the ISS version will be a 1/2 middeck locker configuration with larger volume allocation. The GSM provides a flow rate of 2 sccm for duration of 150 days minimum to support cell science experiment requirements. The usable volume of Air/ CO_2 blend is 285 liters.

Flight Status:

The GSM built for the NASA/Mir Phase I program was launched on *Priroda* in April 1996 and operated successfully on-orbit throughout the two year program supporting cell science investigations.

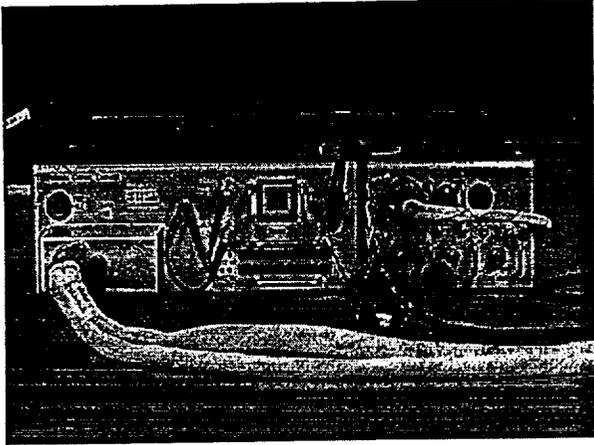


Figure 5. Experiment Control Computer

The Experiment Control Computer (ECC) is a flight certified computer system that is used to control cell culture, tissue engineering, and electrophoresis experiments on earth and in microgravity. Since Biotechnology experiments are continuously operating long-duration experiments, the ECC was designed to minimize the need for crew intervention. The ECC uses an 80486 single board computer and several multifunction electronics boards to perform the following functions: Acquisition and Archiving of Experiment Data, Autonomous Control of Experiment Unique Hardware, Execution of Principal Investigator's Experiment Software, Provides Status and Data Updates to the Crew via Pushbutton LCD and Laptop PC. The ECC has successfully flown on the Shuttle and MIR supporting 9 flight experiments, some lasting as long as 4 months in-flight and will be used during initial Biotechnology experiments on the ISS.

Science Objective:

The Experiment Control Computer (ECC) is designed to provide the computer control resources required for automated, long-duration cell science and tissue engineering investigations on-orbit.

Operational Description:

The ECC is a 486DX2 computer that occupies 1/2 of a middeck locker, and has a high-density 220-pin connector for cable connection to the investigator's experiment equipment. The front panel has two

memory slots for removable (solid state memory cards), and Ethernet and ARCNET connectors.

The ECC provides the interfaces required for communication and control of experiment equipment, execution of the investigator's experiment protocol, and the recording and archiving of experiment data and experiment equipment performance data. The ECC, memory flash cards, and radiation recovery software has successfully operated the EDU space bioreactor for long-duration periods (>130 days) in the Biotechnology System (BTS) facility on Mir.

Flight Status:

The ECC was launched on *Priroda* in April 1996 and operated throughout the *Mir* Phase I Program for a period of 2 years. The ECC has also operated on STS-70, STS-85, STS-86 and STS-91.

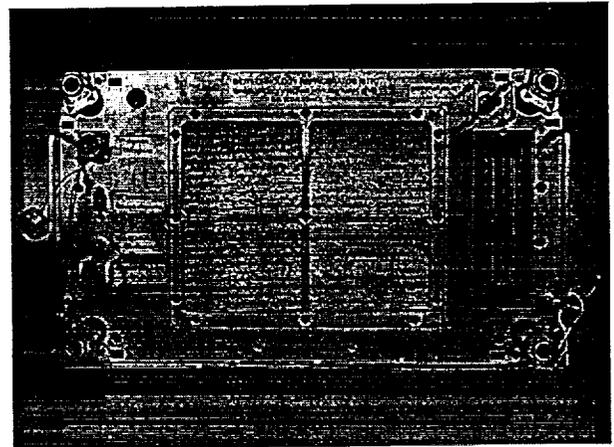


Figure 6. BioTechnology Refrigerator (BTR)

Science Objective:

This hardware is designed to provide low temperature storage for temperature labile culture supplies and biological samples during transport from and to ISS and for on-orbit usage for storing samples obtained during on-orbit cell science and tissue engineering investigations. This controlled-temperature storage volume is easily accessed by the crew for culture medium, reagents, and specimens in support of biotechnology investigations conducted on the ISS.

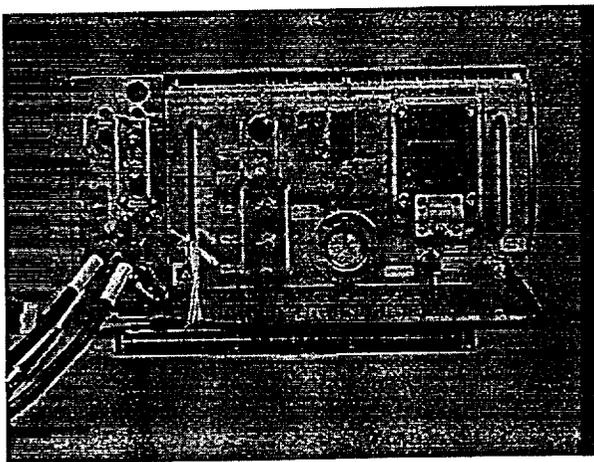
Operational Description:

The BTR is a thermally controlled single middeck locker with a 0.57 ft³ storage volume. Temperatures can range from 4°C to 12°C with a control accuracy of plus or minus 1°C under worst case cabin conditions existing during crew Extra Vehicular Activities. The internal contents are cooled via thermoelectric coolers

and forced convection provided by an internal fan. The BTR provides internal temperature readings to the crew and allows for real-time changes in setpoint temperature and calibration. The BTR uses an accessory temperature data logging device on-orbit to record temperatures throughout the mission. The BTR is designed to operate continuously for duration of up to 365 days. The BTR is presently undergoing upgrades to enhance cooling performance, reliability and accessibility.

Flight Status:

The BTR has successfully launched on STS-86 and STS-89 to support long duration investigations onboard MIR for Increments 6 and 7.



Space Bioreactor

Figure 7. Space Bioreactor System: Engineering Development Unit (EDU)

Science Objective:

This hardware is designed to enable long duration cell culture and tissue engineering research onboard the International Space Station (ISS). The EDU is a bioreactor, which can be inoculated at KSC prior to launch or on-orbit. Cell and media samples can be removed on-orbit through sample ports located on the side and front panels. Once the EDU is powered and the experiment initiated, it remains powered throughout the increment until landing.

Operational Description:

The EDU houses a 125 ml rotating wall perfused vessel in a controlled atmosphere held at 36°C. The EDU has infusion/perfusion capability, a hollow fiber gas exchanger, independent rotation control for vessel outer wall and inner spin filter, and a large window for direct observation and video recording of the vessel itself and

samples. The EDU is supported by two additional pieces of hardware: the Gas Supply Module (GSM) which delivers research grade gases to the bioreactor and the Experiment Control Computer (ECC) which uses memory flash cards to execute the PIs experiment protocol, operate the EDU, and archive experiment data.

Flight Status:

The EDU hosted its first cell science experiment on STS-70 which launched in July of 1995. The EDU subsequently flew on STS-85, and resided onboard MIR for two long duration missions of 128 days and 140 days on Increments 3 and 7.

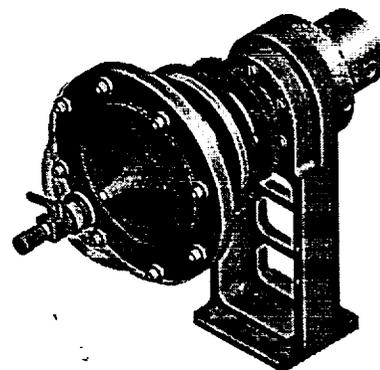
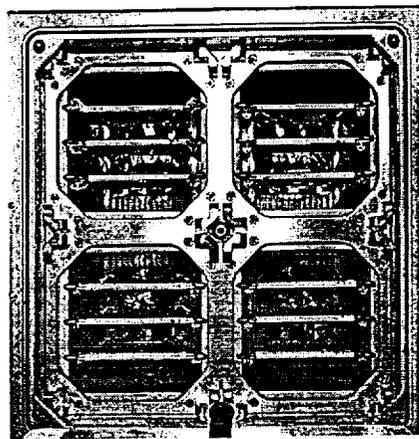
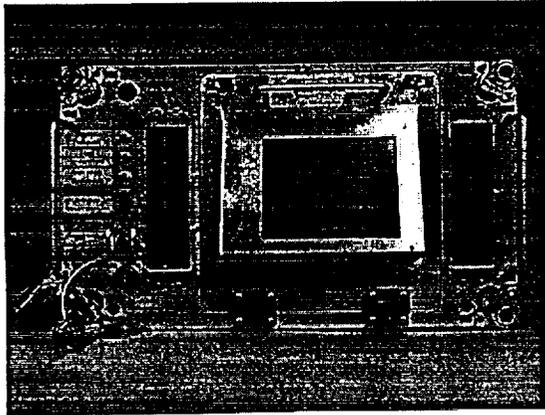


Figure 8. Hydrodynamic Focusing Bioreactor (HFB)

The Hydrodynamic Focusing Bioreactor (HFB) was designed to control the directional movement and removal of air bubbles from the bioreactor vessel on-orbit without degrading the low-shear culture environment or tissue assemblies. The HFB provides unparalleled control over the location of cells and tissues within the bioreactor vessel during operation and sampling. The HFB produces a low-shear fluid environment while a variable hydrofocusing force is used to control the movement, location, and removal of suspended cells, tissue aggregates and air bubbles from the reactor.

Flight Status:

The HFB ground prototype unit has been successfully tested on the KC 135 airplane. The HFB space version is currently in a design and testing phase.



BSTC chambers with Tissue Culture Modules

Figure 9. Space Bioreactor System: Biotechnology Specimen Temperature Controller (BSTC)

Science Objective:

This hardware is a reconfigurable, multi-chamber, temperature controlled static tissue culture apparatus which can accommodate different size experiments. The BSTC is designed so that it can be converted from a 4-chamber configuration to a 1,2 or 3 chamber configuration. Each chamber can be programmed on the ground or on-orbit to a specific experiment profile and is individually controlled for temperature and time.

Temperatures can range from 4°C to 40°C and can be set in .5°C increments. Each chamber can hold a volume of up to three 30 ml Teflon tissue culture modules (TCM) containing media and cells. The BSTC incubates and preserves multiple small cell cultures in microgravity. This design allows for multiple PIs to conduct their unique cell science investigations simultaneously.

Operational Description:

The BSTC is a single middeck locker capable of operating continuously for 180 days. Easy access to these culture modules allows non-invasive microscopic analysis, analysis of media, culture fixation and or passage. The BSTC's front panel touch screen allows the operator to view all systems parameters in either numerical or graphical output. This panel provides a selection of displays and the capability to modify in real-time on-orbit experiment protocols. The control computer contains an AT-compatible CPU card running a 486. Some of the features of this card include: a watchdog timer that resets the system if the program stops running; built-in calendar and clock with an external battery to power the clock during power down. Other sensors will monitor fan speed in each chamber, current, and pressure for spacecraft barometric pressure. Also, each chamber can be charged with custom balanced air/CO2 blends by fitting purge ports onto the face of each chamber door.

Flight Status:

The BSTC has successfully flown on STS-90 and operated onboard Mir during Increment 6 for duration of 128 days.



Astronaut Dr. David Wolf examines tissue in TCM during Increment 6.

A continuously operating Facility design and operation concept was developed in order to meet the science requirements established for the BTF by the Biotechnology Science Working Group (SWG) and the National Research Council (NRC). The SWG and the NRC conducted several reviews of the BTF in 1999 and established levels of science throughput of 4,000 cultures/samples and 3 peer-reviewed publications per year. The continuously operating Facility concept (Figure 10) developed by in the Biotechnology Cellular Program at the Johnson Space Center, enables the BTF

to support this level of investigation and productivity. The concept is based upon (i) using frozen cell samples to inoculate on-orbit bioreactor systems, (ii) reusing of incubator /bioreactor systems repetitively on-orbit, (iii) minimizing Shuttle transport volumes for experiment hardware, and (iv) using dewars to transport frozen biological systems to orbit. In summary, the BTF will be a continuously operating space laboratory on ISS, designed and developed on the basis of science requirements, tested on the ground, and validated in space on the Shuttle and in the Mir BTS Facility. The BTF will enable scientists to conduct microgravity-based biotechnology investigations that will help propel the U.S. into the 21-century as a leader in biotechnology.

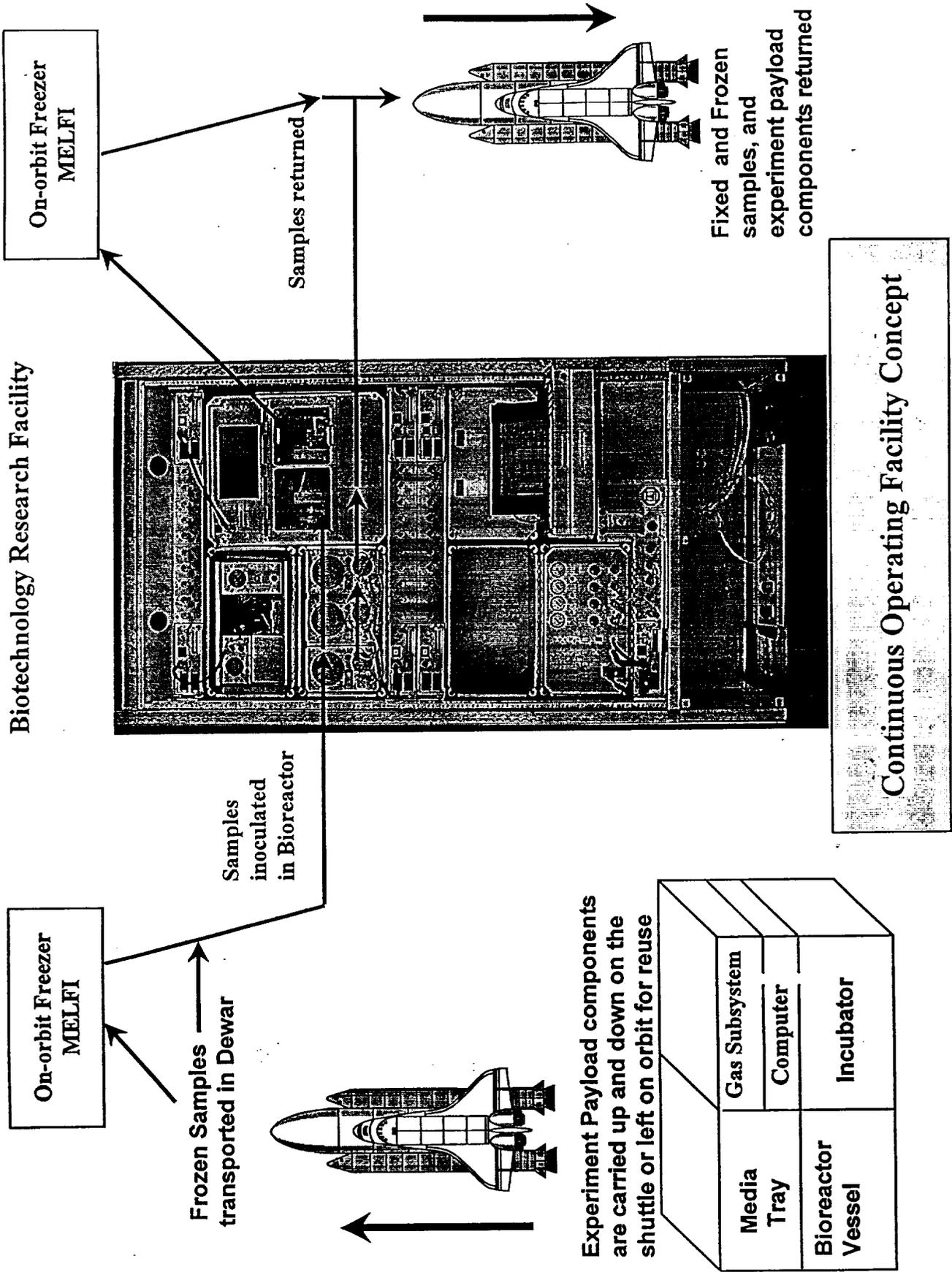


Figure 10
8